# Oral Presentations

## ALLOGENEIC

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### SIROLIMUS AND TACROLIMUS WITHOUT METHOTREXATE AS GRAFT-VS.-HOST DISEASE PROPHYLAXIS AFTER MATCHED, RELATED PERIPHERAL BLOOD STEM CELL TRANSPLANTATION: LOW TRANSPLANT RELATED MORBIDITY AND EXCELLENT GVHD CONTROL

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Sirolimus (Rapamycin, Rap) is a novel immunosuppressant similar to tacrolimus (Tac), however, Rap inhibits T cell function via FKBP12/mTOR and may also inhibit dendritic cell function. Rap is synergistic with Tac and has no overlapping toxicity, allowing their use in combination. We have shown that Rap, Tac and low-dose methotrexate (Mtx) is effective GVHD prophylaxis after URD transplantation. Since Mtx is associated with transplant toxicity and since MRD GVHD rates are lower than URD rates, we hypothesized that Rap and Tac, without Mtx, would provide effective GVHD prophylaxis after MRD PBSCT while minimizing transplant-related morbidity and mortality (TRM). **Methods:** 30 subjects underwent PBSCT from 6/6 HLA-matched siblings(29) or parents(1) after Cy/TBI conditioning. GVHD prophylaxis consisted of Rap (serum level 3-12 ng/ml) and Tac (serum level 5-10 ng/ml). Filgrastim (5 μg/kg) was administered from d+12 until engraftment if needed. **Results:** The median age of subjects was 42 years (range 19-54). Diagnoses were AML(8), MDS(7), CML(7), NHL(6), ALL(1) and ATLL(1). The median times to neutrophil engraftment (>500/μl) and platelet engraftment (>20,000/μl and >100,000/μl) were 14 (range 11-17), 13 (range 10-47), and 19 (range 11-189) days respectively. All patients survived to discharge, at a median of 18 days from day 0 (range 15-54). Gr. II GVHD occurred in 3 patients (10%), involved the skin (3) and gut (1), and resolved with corticosteroids. No patient developed Gr. III-IV GVHD or idiopathic pneumonia syndrome. 4 patients developed thrombotic microangiopathy, but recovered normal renal function when Tac was held. VOD occurred in 3 patients. 1 patient had CMV reactivation and none had invasive fungal infections. Oral mucositis was mild and as a result, 47% of patients required no TPN. The median number of days of TPN use was 6. 9/28 evaluable patients developed chronic GVHD (3 extensive, 6 limited). 6 patients with advanced malignancies relapsed. 22/30 patients remain alive in complete remission. Causes of death include relapse(6), VOD(1) and late pulmonary toxicity(1). The median follow-up is 253 days (range 34-466). Relapse-free and overall survival at day 100 are 93 and 97%, and at 1 year are 70 and 66%. **Conclusions:** Rap and Tac without Mtx is effective for GVHD prophylaxis after MRD PBSCT. Due to Mtx omission, mucositis was reduced, engraftment was prompt and TRM was reduced. This combination is worthy of broader study in allogeneic transplantation.

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### ALLOGENEIC STEM CELL TRANSPLANTATION (SCT) FOR PATIENTS (PTS) WITH THALASSEMIA MAJOR: AN INFERIOR OUTCOME WHEN ANTITHYMOCYTE GLOBLINS (ATG) IS ADDED TO THE CONDITIONING REGIMEN

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**Objectives:** Allogeneic SCT is the only curative modality for pts with Thalassemia Major. Busulfan (BU) and Cyclophosphamide (CY) have traditionally been used as conditioning regimen with satisfactory outcomes. ATG has been added by some investigators in heavily transfused patients in an effort to reduce the risks of rejection. We report here our SCT experience in Thalassemia pts showing an inferior outcome in those who received ATG as part of the conditioning regimen. **Patients and Methods:** From January 1998 through March 2001, 24 Thalassemia pts (11 class I, 11 class II, and 2 class III) underwent allogeneic SCT from HLA-matched related donors at KFSHRC; median age was 4.5 years (range, 2-12.8 years), conditioning was with BU 4 mg/kg/day *p.o* for 4 days, CY 50 mg/kg/day *i.v.* for 4 days, and ATG 30 mg/kg/day *i.v.* for 4 days (group A). Starting June 2001 through May 2003, ATG was removed from the conditioning regimen; and 19 Thalassemia pts (12 class I, 5 class II, and 2 class III) underwent matched related SCT with BU/CY only (group B), median age was 4.5 years (range, 1.5-13.8 years). GVHD prophylaxis was with Cyclosporin and MTX for both groups. Harvested marrow were not manipulated, median CD 34 dose was $8.8 \times 10^6$ (range, $2.3\text{-}17 \times 10^6$) and $8.6 \times 10^6$ (range, $4.9\text{-}14 \times 10^6$) per kg of recipient body weight for groups A and B respectively. Engraftment was assessed by VNTR or FISH on peripheral lymphocytes and/or hemoglobin electrophoresis. **Results:** All pts had primary engraftment; with a median time to ANC = $0.5 \times 10^9$/L of 22 days (range, 14-29 days) and 18 days (range, 11-27 days) for the 2 groups respectively, and a median time to self-sustaining platelet count of = $20 \times 10^9$/L of 18 days (range, 17-68 days) and 32.5 days (range, 16-68 days) for the 2 groups respectively. Four pts in group A (16.6%) developed severe acute GVHD (grade = 3) of the skin, gut, and/or liver versus only one patient in group B (5%). One patient in group A had chronic GVHD versus 2 pts in group B. Secondary graft failure occurred in five pts in group A and in none in group B. For group A, the 5 year actuarial overall and event free survival was 86% and 65 % respectively, and for group B, both the 2 year overall and event free survival was 100%. **Conclusions:** Use of ATG in conditioning of Thalassemia pts undergoing SCT is not beneficial and appears to be associated with a higher incidence of aGVHD and graft failure and with lower survival.

**Table.** *Major Differences in the Outcome of the 2 Groups*

| | Group A | Group B |
|---|---|---|
| Acute GVHD ≥3 | Four | One |
| Chronic GVHD | One | Two |
| Secondary graft failure | Five | None |
| Overall survival | 86% | 100% |
| Event free survival | 65% | 100% |

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### MARROW VERSUS PERIPHERAL BLOOD FOR GENO-IDENTICAL ALLOGENEIC STEM CELL TRANSPLANTATION IN ACUTE MYELOCYTIC LEUKAEMIA: INFLUENCE OF THE DOSE AND THE SOURCE OF STEM CELLS; BETTER OUTCOME WITH RICH MARROW. *ON BEHALF OF THE ACUTE LEUKAEMIA WORKING PARTY (ALWP) OF THE EUROPEAN COOPERATIVE GROUP FOR BLOOD AND MARROW TRANSPLANTATION (EBMT)*

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**Background:** Several studies have compared bone marrow (BM) and peripheral blood (PB) as stem cell sources in allografted patients, but the cell doses infused have not been considered especially for marrow. **Material and methods:** We studied retrospectively on the ALWP/EBMT registry 881 adult patients with Acute Myelocytic Leukaemia (AML), who received a non T depleted allogeneic BM (n = 515) or mobilised PB (n = 366) standard transplant, in CR1, from an HLA identical sibling, over a five year period from January 1994. **Results:** The BM cell dose ranged from 0.17 to $29 \times 10^8$/kg with a median of $2.7 \times 10^8$/Kg. The PB cell dose ranged from 0.02 to $77 \times 10^8$/kg with a median of $9.3 \times 10^8$/kg.